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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-P-0558]

Determination That Oxandrin (Oxandrolone) Tablets, 2.5 Milligrams and 10 Milligrams, Were Withdrawn from Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) has determined that Oxandrin (oxandrolone) tablets, 2.5 milligrams (mg) and 10 mg, were withdrawn from sale for reasons of safety or effectiveness. The Agency will not accept or approve abbreviated new drug applications (ANDAs) for Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg.

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SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved, and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products With Therapeutic Equivalence

Evaluations," which is known generally as the "Orange Book." Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (§ 314.162 (21 CFR 314.162)).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

The anabolic steroid Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, is the subject of NDA 013718, held by Gemini Laboratories LLC (Gemini), and initially approved on July 21, 1964 (for the 2.5 mg strength) and November 5, 2001 (for the 10 mg strength). Oxandrin is indicated as follows: "as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain or to maintain normal weight, to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis."[1]

In a letter dated March 26, 2019, Gemini requested that FDA withdraw approval of NDA 013718 for Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, under § 314.150(c) (21 CFR 314.150(c)), stating that the product was no longer being marketed. Subsequently, on December 16, 2022, FDA notified Gemini that the Agency believes a potential problem

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[1] See Oxandrin (oxandrolone) tablets product labeling (NDA 013718, supplement 023), approved on June 20, 2005, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/013718s023lbl.pdf.

associated with oxandrolone tablets is sufficiently serious that the drug product should be removed from the market, and to enable withdrawal of approval of its application under § 314.150(d). After FDA notified Gemini that it believes the potential problems associated with the drug are sufficiently serious that the drug should be removed from the market pursuant to § 314.150(d), Gemini requested in a letter dated December 19, 2022, that FDA withdraw approval of NDA 013718 for Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg under § 314.150(d). In the *Federal Register* of June 28, 2023 (88 FR 41970), FDA announced that it was withdrawing approval of NDA 013718, effective June 28, 2023.

Novitium Pharma LLC submitted a citizen petition dated April 6, 2022 (Docket No. FDA-2022-P-0558), under 21 CFR 10.30, requesting that the Agency determine whether Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, were withdrawn from sale for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, were withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events.

Our records show that FDA's Endocrinologic and Metabolic Drugs Advisory Committee met and discussed anabolic steroids in January 1984. The advisory committee unanimously concluded that there was no evidence of efficacy for oxandrolone.[2]

As communicated in the product labeling for Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, multiple safety warnings and precautions are associated with the use of this product including peliosis hepatis, sometimes associated with liver failure and intra-abdominal hemorrhage; liver cell tumors, sometimes fatal; and blood lipid changes that are known to be associated with increased risk of atherosclerosis.[3] Per the product labeling, additional warnings with using this product include the risks associated with cholestatic hepatitis, hypercalcemia in patients with breast cancer, and increased risk for the development of prostatic hypertrophy and prostatic carcinoma in geriatric patients.[4] Considering the safety concerns associated with the use of oxandrolone noted in the labeling, the Agency concluded that the benefit-risk profile of the drug product is unfavorable without substantial evidence to support effectiveness.

Based on a thorough evaluation of the information we have available to us and an evaluation of the latest version of the drug products' approved labeling, we have determined that the drug products would not be considered safe and effective if they were reintroduced to the market today. New clinical studies would first need to be conducted to address the concerns described above. Thus, after considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that Oxandrin (oxandrolone) tablets, 2.5 mg and 10 mg, were withdrawn for reasons of safety or effectiveness. Accordingly, the Agency will remove Oxandrin (oxandrolone) tablets,

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[2] See minutes from the January 24 to 25, 1984, advisory committee meeting discussing anabolic steroids, at pg. 7.

[3] See footnote 1.

[4] See footnote 1.

2.5 mg and 10 mg, from the list of drug products published in the Orange Book per § 314.162.

FDA will not accept or approve ANDAs that refer to this drug product.

Dated: September 8, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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